IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT INFRINGEMENT LITIGATION	))))	C.A. No. 05-356-KAJ (consolidated)

NOTICE OF DEPOSITION UNDER FED. R. CIV. P. 30(b)(6)
TO DR. REDDY'S LABORATORIES, INC. AND
DR. REDDY'S LABORATORIES, LTD.

PLEASE TAKE NOTICE that on April 19, 2006 commencing at 9:00 a.m., at the offices of Covington & Burling, 1201 Pennsylvania Avenue, N.W., Washington, D.C. 20004, Plaintiffs Janssen Pharmaceutica N.V., Janssen, L.P. and Synaptech, Inc. (collectively, "Plaintiffs" or "Janssen") will take the deposition upon oral examination of Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. (collectively, "DRL") pursuant to Rule 30(b)(6) of the Federal Rules of Civil Procedure. This deposition upon oral examination will be conducted before an officer authorized to administer oaths and will be recorded by stenographic and videographic means.

Plaintiffs serve this Notice without waiver of its objections to the deficiencies in DRL's document production and other discovery responses concerning the subject matter of the instant Notice, and reserve the right to continue this deposition as necessary in light of any subsequent document production by DRL.

Plaintiffs will take this deposition upon oral examination through one or more officers, directors, managing agents or other persons designated by DRL pursuant to Rule 30(b)(6) of the Federal Rules of Civil Procedure as the person(s) knowledgeable to testify on DRL's behalf concerning the topics identified in Schedule A. DRL is requested to provide

counsel for Plaintiffs with the identity of the individual(s) who will testify regarding each topic at least one week in advance of the deposition. The deposition will continue from day to day until completed with such adjournments as to time and place as may be necessary. You are invited to attend and examine the witness(es).

ASHBY & GEDDES

/s/ Lauren E. Maguire

Steven J. Balick (I.D. #2114)
John G. Day (I.D. #2403)
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Dated: February 21, 2006
166726.1

SCHEDULE A

Definitions

1. As used herein, "DRL" shall mean Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. and all of Dr. Reddy's Laboratories, Inc.'s corporate parents, corporate predecessors and past or present subsidiaries, affiliates, divisions, departments, officers, directors, principals, agents and employees.

2. As used herein, "DRL's ANDA" shall mean DRL's Abbreviated New Drug Application Number 77-593.

3. As used herein, "the Generic Product" shall mean the proposed generic galantamine product that is the subject of DRL's ANDA.

4. As used herein, "the '318 patent" shall mean United States Patent No. 4,663,318.

5. As used herein, "document" shall have the full meaning ascribed to it by the Federal Rules of Civil Procedure and shall include any means for retaining information.

6. As used herein, "FDA" shall mean the United States Food and Drug Administration.

7. As used herein, "Paragraph IV notice" refers to DRL's April 29, 2005 letter to Plaintiffs attached hereto as Exhibit 1.

8. "Person" and "persons" mean any natural person and any business, legal, corporate, or governmental entity, association, or organization.

9. "Alzheimer's Disease" means any diagnosis, illness, or ailment described as being of the Alzheimer's type, including without limitation Senile Dementia of the Alzheimer's Type, and/or Alzheimer's Dementia.

10. "Galantamine" includes without limitation galantamine, galanthamine, and any salt of galatamine, such as galantamine hydrobromide.

Topics of Examination

1. DRL's Paragraph IV notice including, without limitation, the meaning of, basis for, and any evaluation or analysis concerning the statement set forth in the letter that "the '318 patent is invalid."

2. Any evaluation, consideration or discussion conducted by DRL to develop the Generic Product, including the names and responsibilities of all persons who were involved in the evaluation, consideration or discussion by DRL to develop the Generic Product.

3. The decision to file an application with the FDA seeking approval to manufacture and sell a drug product containing galantamine.

4. Any evaluation, consideration or discussion conducted by DRL to market the Generic Product, including the names and responsibilities of all persons who were involved in the evaluation, consideration or discussion by DRL to market the Generic Product.

5. The benefits, including revenues and profits, that DRL projects, anticipates, expects, or forecasts it will obtain should DRL's ANDA receive approval from the U.S. Food and Drug Administration.

6. Marketing strategies, marketing plans, and projected sales for DRL's Generic Product.

7. Each and every contribution and/or input that DRL, or any employee or agent of DRL, has made to the preparation, decision to file, filing and/or prosecution of DRL's ANDA, including: (a) any information relating to regulatory procedures and strategies for obtaining regulatory approval of the Generic Product of DRL's ANDA; (b) any

information comprising, relating to or contained in the 21 U.S.C. § 355(j)(2)(A)(vii)(IV) certifications submitted in connection with DRL's ANDA; and (c) any information comprising, relating to or contained in the statements of factual and legal basis for invalidity, unenforceability, and/or noninfringement included with the notice of these certifications.

8. The factual basis for DRL's proposed assertion that DRL's ANDA is indicated for the treatment of mild to moderate Alzheimer's disease.

9. The circumstances in which DRL first became aware of galantamine as a treatment for Alzheimer's disease, including but not limited to the date on which this occurred and the people involved.

10. The circumstances in which DRL first became aware of the '318 patent, including but not limited to the date on which this occurred and the people involved.

11. Any consideration or evaluation by DRL to develop a drug product containing galantamine for the treatment of Alzheimer's Disease.

12. Identification of all individuals, whether employees of DRL or third parties, having a role in the consideration or evaluation taken by DRL to develop a drug product containing galantamine for the treatment of Alzheimer's disease that is the subject of Topic 11 and a description of those roles.

13. Any effort by DRL to develop any drug product other than the Generic Product set forth in DRL's ANDA.

14. Identification of all individuals, whether employees of DRL or third parties, having a role in the research, development or testing of such a treatment responsive to Topic 13 and a description of those roles.

15. The factual and legal bases for DRL's Second Defense that each and every claim of the '318 patent is invalid under 35 U.S.C. § 101 according to its proof elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

16. The factual and legal bases for DRL's Second Defense that each and every claim of the '318 patent is invalid under 35 U.S.C. § 102 according to its proof elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

17. The factual and legal bases for DRL's Second Defense that each and every claim of the '318 patent is invalid under 35 U.S.C. § 103 according to its proof elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

18. The factual and legal bases for DRL's Second Defense that each and every claim of the '318 patent is invalid under 35 U.S.C. § 112 according to its proof

elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

19. The factual and legal bases for DRL's Second Defense that each and every claim of the '318 patent is invalid under 35 U.S.C. § 116 according to its proof elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

20. The factual and legal bases for Purepac's Second Counterclaim that each claim of the '318 patent is invalid for failure to satisfy one or more of sections 101, 102, 103, 112 and 116 of Title 35 of the United States Code according to its proof elements, including an element-by-element comparison of each asserted claim of the '318 patent to the prior art DRL relies upon and the motivation of one of skill in the art to combine any references under 35 U.S.C. §103, as well as a description of any non-prior art defenses such as lack of enablement, insufficient written description, failure to disclose best mode, or claim indefiniteness under 35 U.S.C. § 112.

21. The identity and location of documents and things concerning the foregoing topics.

22. DRL's document retention policies from 1986 to the present.

23. Persons knowledgeable about the subject matter of the foregoing topics.

166726.1

EXHIBIT 1

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

WCW
MAY - 2 2005

100 SOMERSET CORPORATE BOULEVARD
7TH FLOOR
BRIDGEWATER, NJ 08807
TELEPHONE (908) 203-4900
FAX (908) 203-4970

CERTIFIED MAIL - RETURN RECEIPT REQUESTED (US Recipients)

TO: **President**
Janssen Pharmaceutica NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Chairman & CEO
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933

Synaptech, Inc.
P.O. Box 157
Cold Spring Harbor, NY 11724

FROM: **Dr. Reddy's Laboratories, Ltd.**
Dr. Reddy's Laboratories, Inc.

DATED: **April 29, 2005**

RE: **NOTICE OF PARAGRAPH IV CERTIFICATION RE: GALANTAMINE HYDROBROMIDE ORAL TABLETS EQUIVALENT TO 4, 8 AND 12 MG BASE**

Dear Sirs:

Pursuant to § 505(j)(2)(B)(ii) of the Federal Food, Drug and Cosmetic Act ("the Act") and § 314.95 of Title 21 of the Code of Federal Regulations ("CFR"), please be advised that Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. (collectively "Reddy"), have filed a patent certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Act and § 314.94(a)(12)(i)(A)(4) of Title 21 of the CFR in support of its Abbreviated New Drug Application ("ANDA") with respect to galantamine hydrobromide oral tablets equivalent to 4, 8 and 12 mg base ("the Reddy Galantamine Hydrobromide Tablet Products"). We understand that US Patent Nos. 6,358,527 and 6,099,863 are owned by Janssen Pharmaceutica NV ("Janssen"). We also understand that US Patent No. 4,663,318 is owned by Synaptech, Inc. ("Synaptech").

Reddy provides the following information:

(1) The US Food and Drug Administration ("FDA") has received an ANDA submitted by Reddy containing the required bioavailability or bioequivalence data or information with respect to galantamine hydrobromide tablets;

(2) The ANDA number is 77-593;

(3) The established name of the proposed drug product, as defined in § 502(e)(3) of the Act, is "galantamine hydrobromide";

(4) The active ingredient of the proposed drug product is galantamine hydrobromide, the strength is equivalent to 4, 8 and 12 mg base and the dosage form is an oral tablet;

(5) The U.S. Patent Numbers and expiration dates, as known to Reddy, of the patents alleged to be invalid, unenforceable or not infringed are:

a) Fast-Dissolving Galanthamine Hydrobromide Tablet, US Patent No. 6,358,527 ("the '527 patent"), which is listed in the Electronic "Approved Drug Products with Therapeutic Equivalents" ("Orange Book") as expiring on June 6, 2017;

b) Fast-Dissolving Galanthamine Hydrobromide Tablet, US Patent No. 6,099,863 ("the '863 patent"), which is listed in the Electronic Orange Book as expiring on June 6, 2017; and

c) Method Of Treating Alzheimer's Disease, US Patent No. 4,663,318 ("the '318 patent"), which is listed in the Electronic Orange Book as expiring on the extended date of December 14, 2008.

(6) The information detailed in this letter and the attached memo is supplied for the sole purpose of complying with the above-referenced statutes and regulations, and neither Reddy nor its attorneys waive any attorney-client privilege or attorney work product immunity concerning the subject matter of this communication;

(7) Reddy reserves its right to supplement this letter and the attached memorandum detailing the factual and legal bases for Reddy's assertion of invalidity, unenforceability and/or non-infringement of the '527, '863 and '318 patents, should subsequent investigations reveal additional grounds for asserting invalidity, unenforceability and/or non-infringement.

Reddy is seeking approval from the FDA to market and sell the Reddy Galantamine Hydrobromide Tablet Products for use in the treatment of Alzheimer's disease. Reddy certified with the FDA pursuant to § 505(j)(2)(A)(vii)(IV) of the Act and 21 C.F.R. § 314.94(a)(12)(i)(A)(4) ("Paragraph IV Certification") that the '527, '863, and the '318 patents are invalid, unenforceable or will not be infringed by the manufacture, use, sale, offer to sell or importation into the US of the Reddy Galantamine Hydrobromide Tablet Products for which Reddy has submitted its application.

Offer of Confidential Access: In addition to and not in lieu of the limitations contained in 21 U.S.C. § 355(j)(5)(C)(i)(III) (as amended December 8, 2003) Reddy hereby offers conditional access to only those portions of Reddy's ANDA that, in Reddy's judgment, are needed by Janssen, Johnson & Johnson or Synaptech to determine whether an action under Section 355 should be filed. Access to the information is and shall be limited to only those attorneys acting as outside counsel for Janssen that are needed to evaluate the information and such persons who are to have access shall be identified to Reddy's counsel at Budd Larner, P.C., before access is granted. Such persons so identified shall agree in writing that the information can only be used for the stated purpose. Any tangible form of information derived from a review of the material shall be destroyed, with notice to Reddy, within 45 days of inspection or upon the filing of an action against Reddy, whichever is earlier. Access may only be had at the office of Budd Larner, P.C. at a time and date convenient to the parties.

Pursuant to 21 C.F.R. § 314.95(c)(7), Dr. Reddy's Laboratories, Ltd. authorizes the following agent to accept service of process:

Seshu S. Akula
Dr. Reddy's Laboratories, Inc.
200 Somerset Corporate Blvd., Floor 7
Bridgewater, NJ 08807

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

Attached hereto is a memorandum setting forth Reddy's detailed factual and legal bases supporting the Paragraph IV Certification.

Dr. Reddy's Laboratories, Ltd.

By: _____
Seshu S. Akula
Dr. Reddy's Laboratories, Inc.

MEMORANDUM

TO: President
Janssen Pharmaceutica NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Chairman & CEO
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933

Synaptech, Inc.
P.O. Box 157
Cold Spring Harbor, NY 11724

FROM: Dr. Reddy's Laboratories, Ltd.
Dr. Reddy's Laboratories, Inc.

DATED: April 29, 2005

RE: FACTUAL AND LEGAL BASES FOR DR. REDDY'S LABORATORIES, LTD.'S AND DR. REDDY'S LABORATORIES, INC.'S ASSERTION OF INVALIDITY, UNENFORCEABILITY AND/OR NON-INFRINGEMENT OF US PATENT NOS. 6,358,527, 6,099,863 AND 4,663,318 IN CONNECTION WITH PARAGRAPH IV CERTIFICATION RE: GALANTAMINE HYDROBROMIDE ORAL TABLETS EQUIVALENT TO 4, 8 AND 12 MG BASE

NOTICE OF PARAGRAPH IV CERTIFICATION RE: GALANTAMINE HYDROBROMIDE ORAL TABLETS EQUIVALENT TO 4, 8 AND 12 MG BASE

I. INTRODUCTION

Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. (collectively "Reddy") have submitted an Abbreviated New Drug Application ("ANDA") to the Food and Drug Administration ("FDA") to obtain authorization to market and sell tablets for oral administration containing galantamine hydrobromide, (4a*S*,6*R*,8a*S*)-4a,5,9,10,11,12–hexahydro-3-methoxy-11-methyl-6H-benzofuro[3a,3,2-*ef*][2]benzazepin-

6-ol hydrobromide, equivalent to 4, 8 and 12 mg base ("the Reddy Galantamine Hydrobromide Tablet Products") as the active ingredient for the treatment of symptoms of mild to moderate dementia of the Alzheimer's type.

As an ANDA applicant, Reddy is required to make a certification with respect to any patent published in the US Food and Drug Administration's ("FDA's") "Approved Drug Products with Therapeutic Equivalents" ("Orange Book") relating to the drug product which is the subject of the ANDA.

As of April 29, 2005, there are three US patents listed in the Electronic Orange Book concerning galantamine hydrobromide tablets (equivalent to 4, 8 and 12 mg base). These patents are as follows: US Patent No. 6,358,527 ("the '527 patent"), which is listed in the Electronic Orange Book as expiring on June 6, 2017; US Patent No. 6,099,863 ("the '863 patent"), which is listed in the Electronic Orange Book as expiring on June 6, 2017; and US Patent No. 4,663,318 ("the '318 patent"), which is listed in the Electronic Orange Book as expiring on the extended date of December 14, 2008. Janssen Pharmaceutica N.V. ("Janssen") is listed as the assignee on the face of the '527 patent and the '863 patent. No assignee is listed on the face of the '318 patent. However, the US Patent and Trademark Office's Electronic Patent Assignment database lists Synaptech, Inc. as the assignee.

Reddy certified with the FDA pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug and Cosmetic Act ("the Act") and § 314.94(a)(12)(i)(A)(4) of Title 21 of the Code of Federal Regulations ("CFR") that the '527 patent, the '863 patent and the '318 patent are invalid, unenforceable or would not be infringed by the manufacture, use, sale, offer to sell, or importation into the United States of the Reddy Galantamine

Hydrobromide Tablet Products for which Reddy submitted its ANDA ("Paragraph IV Certification"). This memorandum provides the detailed factual and legal bases supporting Reddy's Paragraph IV Certification.

II. REDDY GALANTAMINE HYDROBROMIDE TABLET PRODUCTS

Reddy manufactures galantamine hydrobromide in India. Upon FDA approval, Reddy's galantamine hydrobromide will be imported into the United States in bulk form and in the form of a tablet containing 5.126 mg galantamine hydrobromide (equivalent to 4 mg galantamine base), 10.253 mg galantamine hydrobromide (equivalent to 8 mg galantamine base), or 15.379 mg galantamine hydrobromide (equivalent to 12 mg galantamine base).

III. DISCUSSION

A. US Patent No. 6,358,527 ("the '527 patent")

1. Overview and Claims

The '527 patent issued on application US Serial No. 09/585,122, filed June 1, 2000, which is a continuation of US Serial No. 09/202,187, filed December 9, 1998, now US Patent No. 6,099,863, which is the national stage application of PCT International Application No. PCT/EP97/02986, filed June 6, 1997, and which claims priority of EP Application No. 96201676, filed June 14, 1996. Paul Marie Victor Gilis and Valentin Florent Victor de Condé are listed as inventors. The claims are listed below:

> 1. A method of treating a disorder selected from dementia, mania or nicotine dependence in a patient in need thereof comprising administering to the patient a tablet comprising as an active ingredient a therapeutically effective amount of galanthamine hydrobromide (1:1) and a pharmaceutically acceptable carrier, wherein said carrier comprises a spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluent, and an insoluble or poorly soluble cross-linked polymer disintegrant.

2. The method of claim 1 wherein the disorder is dementia.

3. The method of claim 2 wherein the disorder is Alzheimer's dementia.

4. The method of claim 1 wherein the disorder is mania.

5. The method of claim 1 wherein the disorder is nicotine dependence.

6. A fast-dissolving galanthamine hydrobromide (1:1) tablet made by (i) dry blending the active ingredient, an insoluble or poorly soluble cross-linked polymer disintegrant and an optional glidant with a diluent comprising a spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25); (ii) optionally mixing a lubricant with the mixture obtained in step (i); (iii) compressing the mixture obtained in step (i) or in step (ii) in the dry state into a tablet; and (iv) optionally film-coating the tablet obtained in step (iii).

2. Claims 1-6 of the '527 Patent would not be Infringed by the Reddy Galantamine Hydrobromide Tablet Products

i. Legal Principles

Tests for infringement of a patent are stated in 35 U.S.C. § 271(a) and (g) as follows:

> (a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.
>
> .....
>
> (g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product, which is made by a process patented in the United States, shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so

made after –

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.

Determining if an accused product infringes the claims of a patent is a two-step process. First, the meaning and scope of the claim must be ascertained. Second, the claim as properly construed must be compared to the accused product. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), aff'd, 517 U.S. 370 (1996).

"In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves." *Tex. Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1201 Fed. Cir. 2002) (quoting *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001). There is a heavy presumption that words in a claim mean what they say and have the ordinary meaning that would be attributed to those words by persons skilled in the relevant art. *Tex Digital*, 308 F.3d at 1202; *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366, (Fed. Cir. 2002). Thus, claim construction analysis must begin with the ordinary meaning of the disputed claim term. *Inverness Medical Switzerland v. Warner Lambert Co.*, 309 F.3d 1373, 1370 (Fed. Cir. 2002); *Tex. Digital*, 308 F.3d at 1201, 1204 ("Consulting the written description and prosecution history as a threshold step in the claim construction process, before any effort is made to discern the ordinary and customary meanings attributed to the words themselves, invites a violation of our precedent ..."). It is well settled that dictionaries and treatises are particularly useful for determining the ordinary meaning of claim terms. *Inverness*, 309 F.3d at 1378; *Tex. Digital*, 308 F.3d at 1202-03.

The specification and prosecution history must be examined in every case to determine whether the presumption of ordinary and customary meaning is rebutted, for example, by use of the claim language in the specification or prosecution history in a manner inconsistent with the ordinary meaning. *Tex. Digital*, 308 F.3d at 1204 ("the presumption in favor of a dictionary definition will be overcome where the patentee, acting as his or her own lexicographer, has clearly set forth an explicit definition of the term different from its ordinary meaning."); *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998).

Further, the presumption will also be rebutted if the inventor has clearly disavowed or disclaimed scope of coverage by using words or expressions of manifest exclusion or restriction in the specification or prosecution history. *Tex. Digital*, 308 F.3d at 1204; *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1324 (Fed. Cir. 2002).

When the intrinsic evidence is unambiguous, it is improper for a court to rely on extrinsic evidence such as expert testimony and inventor testimony, for purposes of claim construction. *Vitronics*, 90 F.3d at 1583; *Mantech Environmental Corp. v. Hudson Environmental Services, Inc.*, 152 F.3d 1368, 1372-73 (Fed. Cir. 1998).

Literal infringement is found where the accused device falls within the scope of the asserted claims as properly interpreted. *Southwall Technologies, Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995). For literal infringement, each limitation in the asserted claim must be found present in the accused device. *General Mills, Inc. v. Hunt-Wesson, Inc.*, 103 F.3d 978, 981 (Fed. Cir. 1997).

The issue of patent infringement is considered separately for each claim of a patent. An independent claim stands alone, while a dependent claim incorporates the

limitations of the independent claim from which it depends. A dependent claim must be narrower than the claim from which it depends and must refer to a previous claim. "A claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all of the limitations of the claim to which it refers." 35 U.S.C. § 112. If the independent claim is not infringed, then the narrower claims that depend from it cannot be infringed. *Wahpeton Canvas Co, v. Frontier, Inc.*, 870 F.2d 1546, 1553 (Fed. Cir. 1989). ("It is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to have been infringed.")

Infringement may also be found under the judicially created doctrine of equivalents. The doctrine of equivalents requires asking whether the accused product contains elements identical or equivalent to each claimed element of the patented invention. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29, 40, 117 S. Ct. 1040, 1049, 1054, (1997). Whether an element is equivalent depends on whether the substitute element matches the function, way, and result of the claimed element or whether the substitute element plays a role substantially different from the claimed element. *Id.*; *Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 608, 70 S. Ct. 854, 856, (1950). (Equivalence can be determined if each of the claimed elements perform substantially the same function in substantially the same way to achieve substantially the same result).

ii. Application of Legal Principles to the '527 Patent Claims

The full text of the claims is provided on pages 3-4 of this memorandum. Claims 1 – 5 of the '527 patent are directed to methods of treatment using galantamine hydrobromide tablets and claim 6 of the '527 patent is directed to a fast-dissolving galantamine hydrobromide tablet.

Every claim of the '527 patent requires the use of an insoluble or poorly soluble cross-linked polymer disintegrant in the galantamine hydrobromide tablet. The Reddy Galantamine Hydrobromide Tablet Products do not contain a cross-linked polymer disintegrant.[1] Therefore, claims 1 – 6 of the '527 patent would not be literally infringed by the making, use, sale or offer for sale in the United States or importation into the United States of the Reddy Galantamine Hydrobromide Tablet Products. Moreover, because the disintegrant in the Reddy Galantamine Hydrobromide Tablet Products would not perform substantially the same function in substantially the same way as the cross-linked polymer disintegrant of claims 1-6 of the '527 patent, the Reddy Galantamine Hydrobromide Tablet Products would not infringe claims 1-6 under the doctrine of equivalents.

B. US Patent No. 6,099,863 ("the '863 patent")

1. Overview and Claims

The '863 patent issued on application US Serial No. 09/202,187, which is the national stage application of PCT International Application No. PCT/EP97/02986, filed June 6, 1997, which claims priority of EP Application No. 96201676, filed June 14, 1996.

[1] We also note that the claims require a spray-dried mixture of lactose monohydrate and microcrystalline cellulose wherein the ratio of lactose monohydrate and microcrystalline cellulose is 75:25, while the Reddy Galantamine Hydrobromide Tablet Products contain a 70:30 mixture of two individually spray-dried excipients: lactose monohydrate (Flowlac-100™) and microcrystalline cellulose (Avicel pH 102™), and not a spray-dried mixture of these excipients.

Paul Marie Victor Gilis and Valentin Florent Victor de Condé are listed as inventors.

The claims of the '863 patent read as follows:

1. A tablet comprising as an active ingredient a therapeutically effective amount of galanthamine hydrobromide (1:1) and a pharmaceutically acceptable carrier, wherein said carrier comprises a spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluent, and an insoluble or poorly soluble cross-linked polymer disintegrant.

2. A tablet according to claim 1 wherein the disintegrant is crospolyvidone or croscarmellose.

3. A tablet according to claim 1 wherein the carrier further comprises a glidant and a lubricant.

4. A tablet according to claim 3 wherein the glidant is colloidal anhydrous silica and wherein the lubricant is magnesium stearate.

5. A tablet according to claim 1 comprising by weight based on the total weight:

   (a) from 2 to 10% galanthamine hydrobromide (1:1);

   (b) from 83 to 93% spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25);

   (c) from 0.1 to 0.4% glidant;

   (d) from 3 to 8% insoluble crosslinked polymeric disintegrant; and

   (e) from 0.2 to 1% lubricant.

6. A tablet according to claim 5 comprising

   (a) about 2 to 10% galanthamine hydrobromide (1:1);

   (b) about 83 to 93% spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25);

   (c) about 0.2% colloidal anhydrous silica;

   (d) about 5% crospolyvidone; and

   (e) about 0.5% magnesium stearate.

7. A tablet according to claim 1 which is film-coated.

8. A tablet according to claim 7 wherein the film-coat comprises a film-forming polymer and a plasticizer.

9. A tablet according to claim 8 wherein the film-coat weighs from about 3% to about 8% of the uncoated tablet core.

10. A process of preparing a tablet according to claim 3 comprising the steps of:

(i) dry blending the active ingredient, the disintegrant and the optional glidant with the diluent;

(ii) optionally mixing the lubricant with the mixture obtained in step (i);

(iii) compressing the mixture obtained in step (i) or in step (ii) in the dry state into a tablet; and

(iv) optionally film-coating the tablet obtained in step (iii).

The '863 patent specification discloses fast-dissolving tablets for oral administration comprising as an active ingredient a therapeutically effective amount of galantamine hydrobromide (1:1) and a pharmaceutically acceptable carrier, characterized in that said carrier comprises a spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluent, and a disintegrant. The '863 patent additionally discloses a direct compression process for preparing these fast-dissolving tablets. The tablets described in the '863 patent have a dissolution of at least 80% after 30 minutes in 500 ml of purified water at 37 °C in Apparatus 2 (USP 23, paddle, 50 rpm). Comparative *in vitro* disssolution studies of various coated and uncoated tablet formulations are also described in the '863 patent.

The '863 patent further discloses that the disintegrant in the formulations of this invention is an insoluble or poorly soluble cross-linked polymer such as, for example, crospolyvidone or croscarmellose. The '863 patent also discloses the amount of said

disintegrant to be from about 3 to 8% (w/w), preferably about 5%. The '863 patent provides experimental data to demonstrate that the dissolution specification for the fast-dissolving tablets was met only if an insoluble or poorly soluble cross-linked polymer was employed as a disintegrant. Specifically, formulations entitled F1, F2, F5, F6, F7a-d are disclosed in the '863 patent. The formulations entitled F1 and F2 do not have an insoluble or poorly soluble cross-linked polymer disintegrant, while the rest of the formulations contain crospolyvidone, an insoluble cross-linked polymer disintegrant. The comparative dissolution data tabulated in col. 7, ln. 5 – col. 8, ln. 22 of the '863 patent demonstrate that the formulations lacking an insoluble or poorly soluble cross-linked polymer disintegrant, *viz.* F1 and F2, do not comply with the dissolution specification, while the formulations containing crospolyvidone, *viz.* F5, F6, and F7a-d, do comply.

The '863 patent also describes various alleged advantages of using a spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25), commercially available as Microcelac™ over the use of lactose monohydrate and microcrystalline cellulose that are not spray-dried, namely reduced tendency to segregate during feeding into the tablet press, and excellent flowability of the diluent.

Additionally, the '863 patent provides the dosage regimen for the oral administration of galantamine hydrobromide tablets to patients in need of galantamine therapy.

2. Claims 1-10 of the '863 Patent would not be Infringed by the Reddy Galantamine Hydrobromide Tablet Products nor by their Manufacture

i. Legal Principles

The legal principles of infringement were set forth in Section III.A.2.i. above.

ii. Application of Legal Principles to the '863 Patent Claims

The full text of the claims is reproduced on pages 9-10 of this memorandum. All claims of the '863 patent require an insoluble or poorly soluble cross-linked polymer disintegrant. Crospolyvidone and croscarmellose are cited in the specification of the '863 patent as examples of such insoluble or poorly soluble cross-linked polymer disintegrants.

The Reddy Galantamine Hydrobromide Tablet Products would not infringe claim 1 of the '863 patent because they do not contain a cross-linked polymer disintegrant.[2] Accordingly, claim 1 of the '863 patent would not be literally infringed by the making, use, sale or offer for sale in the United States or importation into the United States of the Reddy Galantamine Hydrobromide Tablet Products. Moreover, because the disintegrant in the Reddy Galantamine Hydrobromide Tablet Products would not perform substantially the same function in substantially the same way as the cross-linked polymer disintegrant of claim 1 of the '863 patent, the Reddy Galantamine Hydrobromide Tablet Products would not infringe claim 1 under the doctrine of equivalents. As independent claim 1 would not be infringed, literally or under the doctrine of equivalents, claims 2 – 10, which depend from claim 1, would not be infringed, literally or under the doctrine of

[2] We also note that the claims require a spray-dried mixture of lactose monohydrate and microcrystalline cellulose wherein the ratio of lactose monohydrate and microcrystalline cellulose is 75:25, while the Reddy Galantamine Hydrobromide Tablet Products contain a 70:30 mixture of two individually spray-dried excipients: lactose monohydrate (Flowlac-100™) and microcrystalline cellulose (Avicel pH 102™).

equivalents. *Wahpeton Canvas Co., supra.*

C. US Patent No. 4,663,318 ("the '318 patent")

1. Overview and Claims

The '318 patent issued on application US Serial No. 819,141, filed January 15, 1986. No earlier priority is claimed. Bonnie Davis is listed as the sole inventor. The claims are set forth below:

1. A method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

2. A method according to claim 1, wherein the administration is parenteral at a daily dosage of 5-1,000 mg of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

3. A method according to claim 2, wherein said dosage rate is 50-300 mg per day.

4. A method according to claim 1, wherein said administration is oral and is in the range 10-2000 mg per day.

5. A method according to claim 4, wherein said dosage rate of 100-600 mg per day.

6. A method according to claim 1, wherein galanthamine is administered at a dosage rate of 0.1 to 4 mg/kg body weight of a patient, parenterally.

7. A method according to claim 1, wherein galanthamine is administered intracerebroventricularly via an implanted reservoir at a dosage rate of 0.01 to 5.0 mg/kg day.

The '318 patent specification discloses a method for treating Alzheimer's disease by the administration of galantamine. Oral, parenteral and intracerebroventricular administration of galantamine are described. The '318 patent specification discloses improving the cognitive function of patients with Alzheimer's disease. Dosage ranges for oral and parenteral administration are given. Animal tests for predicting the efficacy

of a compound in treating Alzheimer's disease are described. Tablets, capsules and liquid formulations containing galantamine are described in general terms.

2. Claims 2, 3, 6 and 7 of the '318 Patent would not be Infringed by Administration of the Reddy Galantamine Hydrobromide Tablet Products

i. Legal Principles

The legal principles of infringement were set forth in Section III.A.2.i. above.

ii. Application of Legal Principles to the '318 Patent Claims

The phrase, "treating Alzheimer's disease and related dementias," appears in claim 1 of the '318 patent. The customary and ordinary meaning of the term, "treating," is to care for or deal with medically. This term would have been understood by one of ordinary skill in the art to include improving the symptoms of a disease. For example, col. 1, lns. 41-42 of the '318 patent state, "It is an object of the invention to improve the cognitive function of patients with Alzheimer's disease." Deterioration of cognitive function is one of the symptoms of Alzheimer's disease.

Moreover, page 2 of Applicant's Sept. 9, 1986 response in the prosecution of the '318 patent, states that "Applicant currently has experiments underway using animal models which are expected to show that treatment with galanthamine does result in an improvement in the condition of those suffering from Alzheimer's disease." Thus, the claims of the '318 patent are construed to include the improvement of Alzheimer's disease symptoms in Alzheimer's disease patients.

Claims 2, 3 and 6 of the '318 patent are directed to methods for treating Alzheimer's disease and related dementias by parenteral administration of galantamine or a pharmaceutically acceptable salt thereof. Claim 7 is directed to methods for treating

Alzheimer's disease and related dementias by intracerebroventricular administration of galantamine or a pharmaceutically acceptable salt thereof. The Reddy Galantamine Hydrobromide Tablet Products are tablets for oral administration and therefore, their administration would not literally infringe claims 2, 3, and 6, drawn to parenteral administration, and claim 7, drawn to intracerebroventricular administration.

The Reddy Galantamine Hydrobromide Tablet Products also would not infringe claims 2, 3, 6 and 7 of the '318 patent under the doctrine of equivalents. Parenteral and intracerebroventricular administration are carried out with needles and syringes. By contrast, the Reddy Galantamine Hydrobromide Tablet Products, which are tablets, are taken orally. Oral administration does not perform substantially the same function, in substantially the same way as administration by needle or syringe. Use of a needle or syringe requires puncturing the patient's skin and thus, requires careful sterilization of the liquid dosage form. Use of a needle or syringe also bypasses digestive processes of the gastrointestinal tract thereby resulting in different metabolism and half-life of the active ingredient than in the case of orally ingested tablets. Consequently, administration of the Reddy Galantamine Hydrobromide Tablet Products, which are tablets, would not infringe the claims 2, 3, 6 and 7 under the doctrine of equivalents.

3. Claims 1-6 of the '318 Patent would have been Obvious

i. Legal Principles

A US patent is presumed to be valid. 35 USC § 282. A party challenging the patent's validity has the burden of proving invalidity by clear and convincing evidence. *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350 (Fed. Cir. 1984).

35 USC § 103(a), provides:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in § 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. . . .

The ultimate determination of whether an invention would be obvious under 35 USC § 103(a) is a legal question based on underlying findings of fact. *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

The underlying findings of fact under *Graham v. John Deere Co.*, 383 U.S. 1 (1966) include:

1) the scope and content of the prior art;

2) the level of ordinary skill in the art; and

3) the differences between the claimed invention and the prior art.

Analysis under § 103 requires a consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should carry out the claimed process; and (2) whether the prior art would also have revealed that in carrying out the process, those of ordinary skill in the art would have had a reasonable expectation of success. *Velander v. Garner*, 348 F.3d 1359 (Fed. Cir. 2003).

ii. Application of Legal Principles to the '318 Patent Claims

The full text of the claims is set forth on pages 13-14 of this memorandum. Independent claim 1 of the '318 patent is directed to a method for treating Alzheimer's disease and related dementias, which comprises administering to a patient a therapeutically effective amount of galantamine or a pharmaceutically-acceptable acid addition salt thereof. Dependent claims 2 and 3 of the '318 patent are directed to methods for treating Alzheimer's disease, which require respectively the parenteral

administration of a daily dose of 5 - 1,000 mg of galantamine or a pharmaceutically-acceptable acid addition salt thereof, and a daily parenteral dose of 50 - 300 mg of the same. Dependent claims 4 and 5 are directed to methods requiring respectively an oral daily dose of 10 - 2000 mg of galantamine or a pharmaceutically-acceptable acid addition salt thereof, and 100 - 600 mg of a daily dose of the same. Dependent claim 6 is directed to methods requiring a dosage rate of 0.1 to 4 mg/kg administered parenterally.

To determine whether claims 1-6 of '318 patent would have been obvious, the required *Graham* factual inquiries are undertaken, as set forth below.

a. Scope and Content of Prior Art

The scope and content of the prior art are determined as of the date of the invention. 35 USC § 103(a). January 15, 1986, the filing date of the '318 patent, is considered the date of the invention in the absence of other information. As of the date of the invention, the prior art taught that Alzheimer's disease was associated with a deficit in cerebral acetylcholine. It was also recognized that one of the primary therapeutic approaches to treating Alzheimer's disease symptoms in Alzheimer's patients was administration of an acetylcholinesterase inhibitor. It was further known that physostigmine and galantamine were acetylcholinesterase inhibitors. Physostigmine had been administered both orally and parenterally in the treatment of Alzheimer's disease symptoms. Pharmaceutically acceptable salts of galantamine had been used in humans in the clinic for the treatment of short-term memory loss, in reversing the effects of anesthesia, in the treatment of aphasia (loss of speech), and in other areas.

Galantamine hydrobromide was also known at this time to be a substitute for physostigmine in the treatment of cerebral effects of anti-cholinergic substances. It was

also taught in the prior art that galantamine combated the cerebral effects of anticholinergic compounds and that it had a longer duration of action than physostigmine.

Dosage ranges and details for administration of galantamine were available to those skilled in the art. For example, the prior art disclosed 40 mg injections of galantamine hydrobromide solutions, daily 20 mg oral administration of galantamine hydrobromide, and parenteral administration of 0.5 mg/kg of galantamine hydrobromide.

b. Level of Ordinary Skill in the Art

Factors that may be considered in determining the level of ordinary skill in the art include (1) the educational level of the inventor; (2) the type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology and educational level of active workers in the field. *Environmental Designs, Ltd. v. Union Oil Company of California*, 713 F.2d 693 (Fed. Cir. 1983). Here, the educational level of one of ordinary skill in the art would be that of an M.D. of 3 to 5 years' experience having familiarity with clinical studies in the area of human dementia and having an understanding of animal models for diseases like Alzheimer's disease.

c. Differences between the Claimed Invention and the Prior Art

Except for the use of galantamine in the claimed methods, all of the elements of the claims, namely, methods for treating Alzheimer's disease by administration of an anti-cholinesterase agent, had been known in the prior art.

iii. Claim 1 of the '318 Patent would have been Obvious Under 35 USC § 103(a) in View of the Recognized Association of Cerebral Acetylcholine Deficits and Alzheimer's Disease

a. Prior Art Suggested Claimed Process

Independent claim 1 of the '318 patent recites "administration" of galantamine or its pharmaceutically acceptable acid addition salts. At the time of the invention, Alzheimer's disease was known to be associated with deficits of acetylcholine in the brain. The enzyme acetylcholinesterase was known to catalyze the breakdown of acetylcholine and it was also known that a substance which inhibited the activity of the enzyme acetylcholinesterase would lead to a buildup of acetylcholine. By correcting the acetylcholine deficit, such a substance was expected to treat Alzheimer's disease symptoms in Alzheimer's patients.

At the time of the invention, physostigmine was known to have anti-acetylcholinesterase activity. Galantamine was also known to have anti-acetylcholinesterase activity. Anti-cholinergic substances antagonize or reduce the level of acetylcholine. Physostigmine, administered orally or parenterally, was known to treat Alzheimer's disease symptoms in Alzheimer's patients. Galantamine hydrobromide was also known at this time to be a substitute for physostigmine in the treatment of cerebral effects of anti-cholinergic substances. Since galantamine was known to be a substitute for physostigmine in promoting or raising low levels of cerebral acetylcholine caused by anti-cholinergic substances, and because both compounds were known to have anti-acetylcholinesterase activity, the prior art suggested to one of ordinary skill in the art that he or she should carry out the claimed process of treating Alzheimer's disease symptoms in Alzheimer's patients by administration of galantamine.

b. Prior Art Taught that Claimed Process would have Reasonable Likelihood of Success.

The prior art taught that substituting galantamine hydrobromide for physostigmine would have had a likelihood of success in the treatment of the symptoms

of Alzheimer's disease. At the time of the invention, galantamine was being used in patients for reversing short-term memory loss and treating the effects of anesthesia (*See* Applicant's Sept. 9, 1986 response in the prosecution of the '318 patent) and aphasia. Galantamine is known to be safe for use in patients. Physostigmine, while effective for treating Alzheimer's disease symptoms, was possibly toxic, had a short half-life and was difficult to dose. By contrast, galantamine had the following known advantages over physostigmine: 1) lower toxicity; 2) easier dosing; and 3) longer half-life.

The recognized association of cerebral acetylcholine deficits and Alzheimer's disease symptoms in Alzheimer's patients, and the recognized clinical advantages of galantamine over physostigmine, render obvious the administration of galantamine to Alzheimer's patients as recited in claim 1 of the '318 patent.

iv. Claim 1 of the '318 Patent would have been Obvious under 35 USC § 103(a) in view of Known Data on Brain Lesioned Animals

a. Prior Art Suggested Claimed Process

Experimental data on brain-lesioned animals known at the time of the invention provides an independent basis for concluding that claim 1 of the '318 patent is obvious. The prior art recognized that neurons in the region of the brain known as the nucleus basalis de Meynert are responsible for producing acetylcholine. The prior art further recognized that deficiencies in cholinergic neurons in the brain and in the nucleus basalis de Meynert are associated with deficiencies in cognition and learning in Alzheimer's patients. In the '318 patent, at col. 2, lns. 45 – 54, an animal model for Alzheimer's disease is described as follows:

> The following test provides a good animal model for Alzheimer's disease in humans: A selective lesion is placed in a subcortical nucleus (nucleus basalis de Meynert) with a

> resultant cortical cholinergic deficiency, similar in magnitude to that seen in early to moderate stage Alzheimer's disease. Numerous behavioral deficits, including the inability to learn and retain new information, characterizes this lesion. Drugs that can normalize these abnormalities would have a reasonable expectation of efficacyin [*sic*] Alzheimer's disease.

It was also known at the time of the invention that when lesions were made in the nucleus basalis de Meynert, an animal's memory and learning ability were impaired. It was known that administration of the acetylcholinesterase inhibitor physostigmine improved memory and learning in such brain-lesioned animals. As Alzheimer's disease is associated with an acetylcholine deficit and acetylcholinesterase is the enzyme that breaks down acetylcholine, inhibition of that enzyme was recognized by those of ordinary skill in the art to allow acetylcholine to build up and to treat the symptoms of Alzheimer's disease in Alzheimer's patients. Since galantamine hydrobromide was a known substitute for physostigmine in the treatment of cerebral effects of anticholinergic substances, the prior art suggested administering galantamine in place of physostigmine as a method for treating the symptoms of Alzheimer's disease in Alzheimer's patients.

b. Prior Art Taught that Claimed Process would have a Reasonable Likelihood of Success

Substituting galantamine hydrobromide for physostigmine had a reasonable likelihood of success in the treatment of Alzheimer's disease symptoms because galantamine hydrobromide is easier to dose, has a longer half-life and lower toxicity than physostigmine, as discussed in Section III.C.3.iii.b.

For these reasons, the known data on brain-lesioned animals in the prior art make obvious the use of galantamine in the treatment of Alzheimer's disease symptoms and render obvious claim 1 of the '318 patent.

v. Claims 2-6 of the '318 Patent would have Been Obvious under 35 USC § 103(a) in view of Known Data on how to Dose Galantamine in Humans

Claims 2-6 of the '318 patent would have been obvious over the prior art. The prior art discloses 40 mg injections of galantamine hydrobromide solutions for patients. This disclosure falls within the parenteral dosage range of 5 - 1,000 mg of galantamine acid addition salts recited in claim 2, and is close to the dosage range of 50 - 300 mg of galantamine acid addition salts recited in claim 3. Taken together with the art discussed above, claims 2 and 3 of the '318 patent are thereby rendered obvious. The prior art also teaches daily 20 mg oral administration of galantamine hydrobromide, which is within the range recited in claim 4 (10 - 2000 mg daily) and comparable to the range recited in claim 5 (100 - 600 mg daily). Taken together with the art discussed above, claims 4 and 5 of the '318 patent are thereby rendered obvious. Additionally, the prior art discloses parenteral administration of 0,5 mg/kg of galantamine hydrobromide, which is within the range set forth in claim 6 (0.1 to 4 mg/kg). Taken together with the art discussed above, claim 6 of the '318 patent is rendered obvious.

vi. Applicant Failed to Characterize Certain Prior Art Properly and did not Make the Examiner Aware of Certain Prior Art that was Material to Obviousness

The finding that cerebral acetylcholine deficits were associated with the symptoms of Alzheimer's disease in Alzheimer's patients is central to the finding that claims 1 - 6 of the '318 patent are obvious over the prior art. Nevertheless, of all the references considered by the Examiner, only one, Kendall et al. (J. Clinical and Hospital Pharmacy 10, 327-336 (1985)), disclosed the importance of the association of cerebral acetylcholine deficits with the symptoms of Alzheimer's disease in Alzheimer's patients.

Yet, the Applicant selectively quoted from Kendall et al. only the following words, "[...T]he theoretical possibility of developing a long-acting preparation of an agent with good brain penetration[,] and possibly some selectivity of action towards the relevant cortical cholinergic system, must be seen as a major challenge for researchers working on Alzheimer's disease."

The Applicant failed to discuss the cerebral acetylcholine deficit theory in either the '318 patent or its file history. Without any explanation of the association of cerebral acetylcholine deficits and Alzheimer's disease symptoms in Alzheimer's patients, the bare statement in the '318 patent that galantamine and its acid addition salts have anticholinesterase properties is without context.

It is revealing that the inventor, Bonnie Davis, co-authored an article (Mohs et al., "Studies of Cholinergic Drug Effects on Cognition in Normal Subjects and Patients with Alzheimer's disease" in Brain Neurotransmitters in Aging and Age-Related Disorders, Aging, 17, 225-230 (1981)) which states at 225:

> Neuropathological studies indicate that Alzheimer's disease, which is the most common cause of memory loss in elderly people, is a condition that selectively affects cholinergic neurons. Measurements made at autopsy or biopsy of neurochemical markers for different neurotransmitter systems indicate that cholinergic activity is dramatically reduced in Alzheimer's patients and that the activities of other neurotransmitters are reduced to a much lesser extent (cites omitted).
>
> These studies provide rather convincing evidence that a decrease in central cholinergic activity can cause memory impairment. They also suggest that drugs which increase cholinergic activity might alleviate cholinergically based memory deficits and also might improve normal memory performance.

Thus, at the time of filing the application which issued as the '318 patent in 1986, Ms. Davis was clearly aware that treating cerebral acetylcholine deficits of Alzheimer's

disease could be expected to lead to a therapeutic agent for Alzheimer's disease symptoms. Yet, she never disclosed this to the Examiner during prosecution.

It is the duty of the Applicant to provide the Examiner with all material art of which he or she is aware, and to avoid mischaracterizing that art. Failure to comply with that duty may give rise to a claim of inequitable conduct.[3]

vi. Secondary Considerations

Finally, secondary considerations are reviewed in determining whether or not claims 1 – 6 of the '318 patent are obvious. These secondary considerations include commercial success, licensing, long-felt need, copying, near simultaneous invention, and initial skepticism or praise. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Sales figures coupled with market share can be indications of commercial success. *Symbol Technologies, Inc. v. Opticon, Inc.* 935 F.2d 1560 (Fed. Cir. 1991).

Since its introduction in the US, galantamine hydrobromide has held a relatively small share of the Alzheimer's drug treatment market. For the years 2002-2004, that share has been 12 – 14% in dollar figures. Another anti-Alzheimer's drug, rivastigmine, for the same period had a share ranging from 13 – 19%. Sales of yet another anti-Alzheimer's drug, donepezil, for the period have been 58 – 77% in dollar figures. Thus, from 2002-2004, galantamine hydrobromide has not significantly grown its share in the Alzheimer's drug treatment market. Consequently, galantamine hydrobromide has not shown the commercial success necessary to demonstrate the non-obviousness of the

[3] Inequitable conduct has been found where references have been mischaracterized. *Molins PLC v. Textron, Inc.*, 48 F.3d 1172 (Fed. Cir. 1995). Inequitable conduct has also been found where a reference with a more complete combination of relevant features has not been submitted, and references with less complete combinations of features have been supplied instead. *SEL v. Samsung Electronics*, 204 F.3d 1368, 1374 (Fed. Cir. 2000).

claims of the '318 patent. *Ferag AG v. Grapha-Holding AG*, 935 F. Supp. 1238 (D.D.C. 1996).

Satisfaction of a long-felt need is another secondary consideration to be assessed. Here, there is no such satisfaction of a long-felt need. The small and stable market share held by galantamine hydrobromide shows that it did not satisfy such a need. Other Alzheimer's drugs have continued to be prescribed heavily since the launch of galantamine hydrobromide in the US in 2001. Galantamine hydrobromide does not cure Alzheimer's disease.

Since galantamine hydrobromide has not achieved a dominant market share, nor satisfied a long-felt need, these secondary considerations fail to rebut the *prima facie* case of non-obviousness of claims 1-6 of the '318 patent.

CERTIFICATE OF SERVICE

I hereby certify that on the 21st day of February, 2006, the attached **NOTICE OF DEPOSITION UNDER FED. R. CIV. P. 30(b)(6) TO DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES, LTD.** was served upon the below-named counsel of record at the address and in the manner indicated:

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